

## **REMARKS/ARGUMENTS**

Prior to the amendments presented herewith, claims 1-13, 15-25, 27-29, 31, 33-73 and 75-86 were pending. Claims 13, 25 and 58 are being amended. Claims 11, 12, 15-24, 33-57, 59-68, 70-73 and 75-86 are being withdrawn. Claims 1-10, 14, 26, 30, 32 and 74 have been cancelled. Accordingly, after the present amendments have been entered, claims 13, 25, 27-29, 31, 58 and 69 will be pending.

### **1. Election in Response to Restriction**

In the Office Action, the Examiner indicates that the restriction requirement is made final and has required that the term “carbocyclic ring” in the definition of R<sub>3</sub> and R<sub>4</sub> be substituted with the term “benzo ring.” The cancellation of claim 1 renders the rejection moot. In addition, claims 11, 12, 15-24, 33-57, 59-68, 70-73 and 75-86 are withdrawn as being directed to non-elected subject matter pursuant to 37 C.F.R. 1.142(b). All of the pending claims now read on the elected subject matter.

Applicants reserve the right to petition for rejoinder under 37 C.F.R. § 1.144 with regard to the non-elected claims, once the elected claims are placed in condition for allowance. Applicants also reserve the right pursuant to 35 U.S.C. § 121 to file one or more divisional applications directed to the non-elected subject matter during the pendency of the present application.

### **2. Information Disclosure Statements**

Applicants thank the Examiner for indicating that the Forms 1449 filed on February 23, 2005, August 2, 2005, September 14, 2005 and April 6, 2006 have been considered. However, Applicants note that an initialed copy of the Form 1449 filed on August 2, 2005 did not accompany the Office Action. An initialed copy of the Form 1449 is requested (copy attached).

Applicants also note that six (6) supplemental Information Disclosure Statements (“IDSs”) were filed on August 15, 2006, September 7, 2006, September 26, 2006, November 15, 2006, January 8, 2007 and January 23, 2007, in connection with the present application. Initialed copies of these Forms 1449 also are requested.

### 3. Claim rejections under 35 USC §102

Claims 1-8, 10-11, 13 and 86 are rejected as being anticipated by Kozhevnikov *et al.*, Tr. Perm. Sel.-Khoz. Inst. (1971), 79, 66-72 from ref. Zh., Khim. 1972, Abstr. No. 9Zh404). In addition, claims 1-8, 10, 11, 13, 27 and 29 are rejected as being anticipated by Chenard *et al.*, *J. Med. Chem.* (2001), 44, 1710-17. Further, claims 1-8, 10, 11, 13, 27 and 29 are rejected as being anticipated by Pattanaik *et al.*, *Indian Journal of Chemistry, Section B* (1998), 37B (12), 1304-06. Finally, claims 1-13, 27 and 29 are rejected as being anticipated by Chenard *et al.* (EP 0900568 A2).

Claims 13 and 58 are being amended to recite that R<sub>1</sub> is a substituted or unsubstituted benzyl. Since none of the art cited by the Examiner teaches or suggests the presently claimed compounds wherein R<sub>1</sub> is benzyl, the rejection of claims 1-8, 10-11, 13 and 86 is believed to be overcome.

In light of the foregoing, the rejection of claims 1-8, 10-11, 13 and 86 under 35 USC §102 should be withdrawn.

### 4. Claim rejections under 35 USC §112, second paragraph

With respect to the term "substituted," the Examiner appears to suggest that the claims are indefinite because the claims do not articulate the particular moieties which facilitate substitution. However, the claim need not list every possible substituent for one of ordinary skill in the art to know what is within the scope of the claim. See *Ex parte* Lani S. Kangas, Mieczyslaw H. Mazurek, Kurt C. Melancom, Walter R. Romanko, and Audrey A. Sherman, Appeal No. 2002-0250 (BPAI 2002) (copy attached). The claim may be broad in terms of possible R groups, but that alone does not make the claim indefinite. MPEP 2173.04.

In addition, the specification provides guidance in the interpretation of the term "substituted". Specifically, the specification at paragraph [0098] states:

In general, a non-hydrogen substituent may be any substituent that may be bound to an atom of the given moiety that is specified to be substituted. Examples of substituents include, but are not limited to, aldehyde, alicyclic, aliphatic, alkyl, alkylene, alkylidene, amide, amino, aminoalkyl, aromatic, aryl, bicycloalkyl, bicycloaryl, carbamoyl, carbocyclyl, carboxyl, carbonyl group,

cycloalkyl, cycloalkylene, ester, halo, heterobicycloalkyl, heterocycloalkylene, heteroaryl, heterobicycloaryl, heterocycloalkyl, oxo, hydroxy, iminoketone, ketone, nitro, oxaalkyl, and oxoalkyl moieties, each of which may optionally also be substituted or unsubstituted.

Definitions for the term “substituent” can also be found in the literature. For example, Hawley’s Condensed Chemical Dictionary 1056 (13<sup>th</sup> Ed. 1997) defines “substituent” as “[a]n atom or radical that replaces another in a molecule as the result of a reaction” (see attached).

Accordingly, one of ordinary skill in the art would understand the bounds of the term “substituted” as it is used in the present claims. Therefore, the rejection is improper and should be withdrawn. However, solely to advance prosecution of the present invention, claims 13 and 58 are being amended to recite particular substituents for R<sub>1</sub>, R<sub>9</sub> and R<sub>12</sub>. Support for the amendment can be found, for example, in the specification at paragraphs [0098]. and [0200], and original claim 13

The Examiner also indicates that use of the phrase “heteroaryl comprising a nitrogen ring atom” is indefinite. Applicants respectfully disagree. The specification at paragraph [0079] clearly defines “heteroaryl” as a cyclic aromatic group having 5 or 6 ring atoms, wherein at least one ring atom is a heteroatom. The specification goes on to define “heteroatom” at paragraph [0081] as an atom that is not carbon (such as, for example, nitrogen, oxygen and sulfur). Accordingly, those skilled in the art would readily understand that the phrase “heteroaryl comprising a nitrogen ring atom” refers to cyclic aromatic groups having 5 or 6 ring atoms, wherein at least one ring atom is nitrogen and the other ring atoms are either carbon or a further heteroatom. A similar analysis applies to the phrase “cycloalkyl comprising a nitrogen ring atom” (*see*, specification at paragraphs [0073], [0081] and [0085]). In light of the foregoing, the rejection is believed to be improper and should be withdrawn.

In addition, the claims are rejected because the phrase “U is a moiety providing 1-6 atom separation” is allegedly indefinite. However, those skilled in the art would readily understand that U is a “linker” that joins V to the ring carbon atom of the compound of Formula XXIX. As such, the atoms in the direct chain of atoms that link V to the ring are the atoms that provide the separation between V and the ring. Furthermore, Applicants provide ample descriptions of what may be used as U. *See, e.g.*, Specification at paragraphs [0232]-[0244]. However, solely to advance prosecution of the present application, the claims are being amended to recite particular

groups for U. In light of the foregoing, the rejection should be withdrawn.

The claims are also rejected because the phrase “V comprises a basic nitrogen atom that is capable of interacting with a carboxylic acid side chain of an active site residue of a protein” is allegedly indefinite. Applicants respectfully disagree. Applicants suspect that the rejection is based on the fact that the Examiner is unclear whether the ring nitrogen of the species described at paragraph [0240] is capable of interacting with the carboxylic acid. However, those skilled in the art would readily appreciate that the ring nitrogen atoms of the moieties of paragraph [0240] (including the piperidine) do *not* constitute the basic nitrogen atom required by the claims. Since U requires at least one atom, the ring nitrogen atom of the moieties of paragraph [0240] necessarily must be read as being part of U. Accordingly, the ring nitrogen atom of the moieties cannot constitute the basic nitrogen atom required of V. The fact that the aforementioned ring nitrogens do not provide the necessary basic nitrogen is precisely why moieties of the type specified in paragraph [0241] can be used in connection with the present invention, even though those moieties do not even contain a ring nitrogen. However, solely to advance prosecution of the present application, the claims are being amended to recite particular groups for V. Accordingly, the rejection should be withdrawn.

Claims 25, 84 and 85 are rejected because the phrase “the ring formed by J, K, L and M comprises substituents that form a ring fused to or bridged to the ring formed by J, K, L and M” is allegedly indefinite. Applicants respectfully disagree. Each of J, K, L and M is defined as being CR<sub>12</sub>. Those skilled in the art would readily understand that two R<sub>12</sub> groups, together with the atoms to which they are attached, can be linked to form a ring. When the two R<sub>12</sub> groups are on adjacent atoms in the ring formed by J, K, L and M, the resulting ring is fused to the ring formed by J, K, L and M. When the two R<sub>12</sub> groups are not on adjacent atoms in the ring formed by J, K, L and M, the resulting ring is bridged to the ring formed by J, K, L and M. Still, claims 13 and 25 are being amended to more clearly provide for embodiments wherein “two R<sub>12</sub> [can be] taken together to form a ring.” Accordingly, the rejection should be withdrawn.

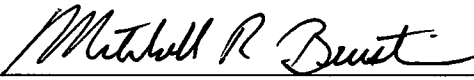
**CONCLUSION**

Applicants earnestly believe that they are entitled to a letters patent, and respectfully solicit the Examiner to expedite prosecution of this patent application to issuance. Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned.

Respectfully submitted,

TAKEDA SAN DIEGO, INC.

Dated: February 12, 2007

By:   
Mitchell R. Brustein  
Reg. No. 38,394

Customer No. **32793**  
Takeda San Diego, Inc.  
10410 Science Center Drive  
San Diego, CA 92121  
Telephone: (858) 622-8528  
Facsimile: (858) 550-0992